Abstracts

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Age-Adjusted D-Dimer Cutoff Levels to Rule Out Pulmonary Embolism: The ADJUST-PE Study

Righini M, Van Es J, Den Exter PL, et al. JAMA 2014;311:1117-24.

Conclusions: Compared with a fixed D-dimer cutoff 500 μg/L, a combination of pretest clinical probability assessment with age-adjusted D-dimer cutoff is associated with a large number of patients in whom PE can be considered ruled out with a low likelihood of subsequent clinical venous thromboembolism (VTE).

Summary: In patients with currently suspected acute pulmonary embolism (PE) sequential diagnostic tests, such as clinical probability assessment, plasma D-dimer measurement, compression ultrasound, computed tomography pulmonary angiography (CTPA), or ventilation-perfusion lung scanning is used as a standard diagnostic approach. D-dimer testing has also been evaluated extensively for the exclusion of PE particularly in outpatients (Righini M et al, J Thromb Haemost 2008;6:1059-71). However, D-dimer levels normally increase with age. Therefore the clinical usefulness of the test may be limited in older patients. Previously it was found that D-dimer testing was able to rule out PE in 60% of patients younger than 40 years, but only 5% of patients older than 80 years (Righini M, et al. J Thromb Haemost 2007;5:1869-77). The authors here have previously retrospectively determined a progressive D-dimer cutoff adjusted for age in a sample of 1712 patients. They defined optimal age-adjusted cutoff as the patients age multiplied by 10 in patients 50 years or older (Douma RA et al, BMJ 2010;340:c1475). To confirm the utility of this cutoff a multicenter, multinational, prospective management outcome study was conducted in 19 centers in Belgium, France, The Netherlands, and Switzerland between January 1, 2010 and February 28, 2013. Consecutive patients who presented to the emergency department with clinical suspected PE were assessed by a sequential diagnostic strategy based on the clinical probability assessmeny with the revised Geneva score or the 2-level Wells score for PE; high sensitive D-dimer measurement; and CTPA. Patients with D-dimer values between the conventional cutoff of 500 μg/L and their age-adjusted cutoff did not undergo CTPA and were left untreated and followed for 3 months. Primary outcome was the failure rate of the diagnostic strategy, defined as the rate of adjudicated VTE events during the 3 month follow-up period among patients not treated with anticoagulants on the basis of a negative age-adjusted D-dimer cutoff result. Of the 3346 patients with suspected PE included in the study, the prevalence of PE was 19%. Among the 2898 patients with a nonhigh or an unlikely clinical probability of PE, 817 patients (28.2%) had a D-dimer level lower than 500 μg/L (95% CI, 26.6%-29.9%), and 337 patients (11.6%) had a D-dimer between 500 μg/L and their age-adjusted cutoff (95% CI, 10.5%-12.9%). The 3-month failure rate in patients with a D-dimer level higher than 500 μg/L but below the age-adjusted cut-off was 1 of 331 patients (0.3%; 95% CI, 0.1%-1.7%). Among 776 patients 75 years or older, there were who 673 had a non-high clinical probability, using the age-adjusted cutoff instead of the 500 μg/L cut-off. This increased the proportion of patients in whom PE could be excluded on the basis of D-dimer from 43 of 673 patients (6.4%; 95% CI, 4.8%-8.5%) to 200 of 673 patients (29.7%; 95% CI, 26.4%-33.3%), with no additional false-negative findings.

Comment: It is important to remember that the findings for D-dimer for exclusion of PE, as presented in this study, still applies only to outpatients. However, it does appear that the use of age-adjusted D-dimer cutoffs in clinical practice for evaluation of PE in outpatients has potential for improved cost effectiveness and improved quality of care, particularly in older patients. Additional studies to address these particular issues will be required before wide-spread adoption of age-adjusted D-dimer cutoffs can be expected.

Progression Rate and Ipsilateral Neurological Events in Asymptomatic Carotid Stenosis

Hirt LS Stroke 2014;45:702-6.

Conclusions: Rapid rates of progression of carotid artery stenosis portend significantly increased risk of future ipsilateral neurologic events.

Summary: About 3.6% of the general population has a ≥50% asymptomatic carotid artery stenosis with attendant increased risk of future stroke. Given that recent evidence suggests stroke risk is fallowing with carotid stenosis identifying those lesions with a particular high risk of stroke would be important. Potential risk factors for stroke with carotid artery stenosis include the degree of carotid narrowing, plaque morphology, plaque hemorrhage, detection of cerebral microemboli, and progression rates of luminal narrowing. Stenosis progression occurrs in 5% to 20% of patients with asymptomatic carotid stenosis (Norris JW et al, Stroke 1992;23:483-5, and Lewis RF et al, Ann Intern Med 1997;127:13-20). In this study the authors sought to evaluate the yearly rate of change of carotid luminal narrowing as a risk factor for ipsilateral ischemic neurologic events in patients with ≥50% asymptomatic carotid stenosis. Patients were those who took part in the deferred endarterectomy arm of the Asymptomatic Carotid Surgery Trial (ACST). Secondary aims were to establish the annual incidence of progression and regression of luminal narrowing and identify other risk factors associated with ipsilateral neurological events in these patients. This was a retrospective analysis of data derived from the deferred endarterectomy arm of the Asymptomatic Carotid Surgery Trial. Patients were followed for ≥5years with serial carotid duplex examinations. Data were derived from information obtained at randomization and annual follow-up visits with carotid duplex studies. Potential risk factors for ipsilateral neurological events were analyzed in Poisson regression models. There were data from 1469 patients included. 244 had ipsilateral events; 240 had ipsilateral carotid surgery; 370 died from nonstroke causes and 82 had an asymptomatic carotid occlusion. The annual incidence of contralateral symptoms showed a significant independent association with ipsilateral neurological events. Ipsilateral events were associated with higher rates of progression over 1 year but not with low progression rates.

Comment: The results of this study have significant implications for clinical practice. Duplex measurements demonstrating a slow rate of progression of asymptomatic carotid stenosis should not be interpreted as a sign of increase risk of future neurologic events. Faster rates of progression are associated with an increased risk of future ipsilateral neurologic events and perhaps therefore can be used as one of the variables in the decision to perform intervention for asymptomatic carotid stenosis.

Clinical and Cost-Effectiveness of Compression Hosiery Versus Compression Bandages in Treatment of Venous Leg Ulcers (Venous leg Ulcer Study IV, VenUS IV): A Randomised Controlled Trial

Ashby R, Gabe R, Ali S, et al. Lancet 2014;383:871-9.

Conclusions: Two-layer compression hosiery and four-layer bandages are equally effective in healing venous leg ulcers.

Summary: Four-layer multi-component compression bandages are regarded by many as the gold standard compression system to treat venous leg ulceration (O'Meara S et al, Cochrane Database Syst Rev 2012;(1):CD000265). Two-layer compression hosiery systems have also been marketed for treatment of venous leg ulcers. They are designed to deliver 40 mm Hg of compression at the ankle when both layers understocking and overstocking are worn together. Two-layer hosiery is less bulky than a four-layer bandage and can be more easily worn with shoes and might enhance ankle or leg mobility and therefore patient adherence. There is however, little evidence from randomized controlled trials of the effectiveness of two-layer hosiery for ulcer healing. There have been no trials comparing two-layer hosiery and four-layer bandages. In this study the authors sought to compare the clinical effectiveness and cost effectiveness of two-layer hosiery with four-layer bandages for healing of venous ulcers. This was an open randomized control trial with two parallel groups conducted in 34 centers in England and Northern Ireland. Centers were community nurse teams or services, family doctor practices, leg ulcer clinics, tissue viability clinics or services, and wound clinics. Study participants were 18 years of age or older with a venous leg ulcer and an ankle brachial pressure index of at least 0.8, and were able to tolerate high compression. Participants were manually allocated 1:1 to receive two-layer compression hosiery or a four-layer bandage using a remote randomization service and a prevalidated computer randomization program. Stratification was by ulcer duration and ulcer area with permuted blocks. The primary end point was time to ulcer healing with a maximum follow-up of 12 months. Participants and health-care providers were not masked to treatment allocation but the primary end point was measured by masked assessment of photographs. Primary analysis was intention to treat with Cox regression, with adjustment for ulcer area, ulcer duration, physical mobility and center. Secondary end points were unmasked outcome assessment, unmasked measurement of